What is claimed is:

1. An isolated nucleic acid fragment encoding a PAIGB polypeptide selected from the group consisting of:

(a) an isolated nucleic acid fragment encoding SEQ ID NO:2,4,6, 8 and 10,

(b) an isolated nucleic acid fragment encoding an amino acid sequence having at least 85% identity with the SEQ ID NO: 2,4,6, 8 and 10,

(c) an isolated nucleic acid molecule that hybridizes with the isolated nucleic acid fragment of (a) under hybridization conditions of 6X SSC (1M NaCl), 45 to 50 % formamide, 1 % SDS at 37 °C, and a wash in 0.5X to 1X SSC at 55 to 60 °C; and,

(d) an isolated nucleic acid fragment that is complementary to (a), (b) or (c).

2. The isolated nucleic acid fragment of Claim 1 selected from the group consisting of SEQ ID NO:1, 3, 5, 7, and 9.

3. The isolated nucleic acid fragment of Claim 1 wherein the isolated nucleic acid fragment is DNA.

4. The isolated nucleic acid fragment of Claim 1 wherein the isolated nucleic acid fragment is RNA.

5. The nucleic acid fragment of Claim 1 wherein the nucleic acid fragment encodes a polypeptide which is involved in PTH signaling pathway.

6. The nucleic acid fragment of Claim 1 which when overexpressed induces bone forming activity in bone tissues.

7. The isolated nucleic acid fragment of Claim 1, which is overexpressed in response to intermittent PTH administration.

8. A polypeptide encoded by the isolated nucleic acid fragment of Claim 1.

9. A polypeptide of Claim 8 selected from the group consisting of SEQ ID NO: 2,4,6, 8 and 10.

10. The polypeptide of Claim 8, which is involved in PTH signaling pathway.

11. The polypeptide of Claim 8 which when overexpressed induces bone forming activity in bone tissues.

12. The polypeptide of Claim 8 which is overexpressed in response to intermittent PTH administration.

13. A chimeric construct comprising the isolated nucleic acid fragment of Claim1 operatively linked to suitable regulatory sequences.

14. A host cell transformed with the chimeric construct of Claim 13.

15. The host cell of Claim 14 wherein the host cell is selected from the group consisting of an eukaryotic, a prokaryotic cell, and a multicellular organism.

16. The host cell of Claim 15 wherein the host cell is a mammalian cell.

17. The host cell of Claim 16 wherein the host cell is a mammalian osteoblast cell.

18. The host cell of Claim 16 wherein the host cell is selected from the group consisting of a COS-7 (monkey kidney), 293 (human kidney), CHO (hamster ovary), HepG2 (human liver), HeLa (human cervical), NIH3T3 (mouse fibroblast), Primary osteoblasts, TE-85 (human osteoblast), MG-63 (human osteoblast), SAOS-2 (human osteoblast), UMR 106 (rat osteoblast), ROS 17/2.8 (rat osteoblast), MC3T3

(mouse osteoblast), and U2OS (human osteoblast)).

19. The host cell of Claim 15 wherein the host cell is a human osteoblast cell.

20. The host cell of Claim 15 wherein the host cell is *E.coli.*

21. The host cell of Claim 20 wherein the host cell is selected from the group consisting of DH5alpha, BL21, and DH10B.

22. The host cell of Claim 15 wherein the host cell is a yeast cell.

23. The host cell of Claim 22 wherein the host cell is selected from the group consisting of Schizasaccharomyces, *Saccharomyces Cerevisice*, *Pichia Pastoris*, and *Pichia Methanolic.*

24. The host cell of Claim 15 wherein the host cell is an insect cell.

25. The host cell of Claim 24 wherein the host cell is selected from the group consisting of SF, SF21 – *Spodoptera Frugiperda*, S2 Schneider Cells, and High Five Cells from *Trichoplusia ni* egg.

26. A vector comprising the nucleic acid fragment of Claim 1.

27. The vector of Claim 26, wherein the vector is a plasmid.

28. A transformed cell comprising the vector of Claim 26.

29. The transformed cell of Claim 28, wherein the host microorganism is selected from the group consisting of eukaryotic, prokaryotic cell, and multicellular organism.

30. The transformed cell of Claim 29, wherein the host microorganism is a mammalian cell.

31. The host cell of Claim 30 wherein the host cell is a mammalian osteoblast cell.

32. The transformed cell of Claim 28, wherein the host microorganism is E.coli.

33. The transformed cell of Claim 28, wherein the host microorganism is a yeast cell.

34. A method of obtaining a nucleic acid fragment encoding the polypeptide of Claim 8, the method comprising:

(a) probing a genomic library with all or a portion of a nucleic acid fragment as set forth in SEQ ID NO:3; SEQ ID NO:5, SEQ ID NO: 7, or SEQ ID NO:9.

(b) identifying a DNA clone that hybridizes with the nucleic acid fragment of step (a); and

(c) determining the sequence of the nucleic acid fragment that comprises the DNA clone identified in step (b).

35. A method of obtaining a polypeptide of Claim 8, the method comprising:

(a) introducing the vector of claim 26 into a suitable host cell;

(b) culturing the resulting cell so as to produce the polypeptide;

(c) recovering the polypeptide produced in step (b); and

(d) isolating the polypeptide so recovered.

36. A method for detecting the presence of a nucleic acid fragment of Claim 1 in a biological sample comprising: (a) contacting the biological sample with nucleic acid fragment of Claim 1; (b) determining whether the nucleic acid fragment binds to a nucleic acid molecule in the biological sample to thereby detect the presence of a nucleic acid fragment of Claim 1 in the sample.

37. An antibody that specifically binds to one or more epitopes of a PAIGB polypeptide of Claim 8.

38. A composition for regulating bone-forming activity in a mammal comprising at least one of (i) nucleic acid fragment of Claim 1, (ii) polypeptide of Claim 8, (iii) an antibody formed from such polypetides or portions thereof.

39. A composition according to Claim 38, wherein said PAIGB is from human osteoblast cells.

40. A composition according to Claim 38, wherein the bone forming activity is the regulation of bone growth.

41. A composition according to Claim 38, wherein the bone forming activity is regulation of bone density.

42. The composition according to Claim 38, wherein the PAIGB has the amino acid sequence set forth in SEQ ID NO: 2,4,6,8, and 10.

43. An agent that alters the expression of PAIGB gene or polypeptide.

44. The agent of Claim 43 wherein the agent is polynucleotide.

45. The agent of Claim 43 wherein the agent is polypeptide.

46. The agent of Claim 43, wherein said agent is chemical small molecule.

47. The agent of Claim 43, wherein said agent is a peptide.

48. The agent of Claim 43 wherein the agent induces bone-forming activity.

49. The agent of Claim 43 wherein the agent exhibits at least one of the

following: (a) an induction in bone forming activity, (b) an increase in osteoblastic differentiation from osteoprogenitor cells, (c) an increase in osteoblastic activity, (d) an increase in osteoblast profilteration, or (e) a decrease in osteoblast apoptosis.

50. A composition comprising the agent of Claim 43.

51. A method for determining whether an agent alters the expression of PAIGB mRNA, the method comprising: a) measuring the level of PAIGB mRNA present in a test sample not contacted with the agent; b) measuring the level of PAIGB mRNA present in the test sample contacted with the agent; and c) determining that the agent alters the expression of PAIGB mRNA when the level of PAIGB mRNA measured in step a) differs from the level of PAIGB mRNA measured in step b).

52. A method of Claim 51 where in the test sample is selected from the group consisting of bone tissue biopsy, bone marrow aspirates, and joint fluids.

53. A method for screening agents for effectiveness in altering expression of a nucleic acid fragment of Claim 1, the method comprising a) contacting a test sample comprising nucleic acid fragment of Claim 1 with an agent under condition suitable for the expression of the nucleic acid fragment of Claim 1, b) detecting altered expression of the nucleic acid fragment of Claim 1, and c) comparing the expression of the nucleic acid fragment of Claim 1 in the presence of varying amounts of the agent and in the absence of the compound.

54. A method of Claim 53 where in the test sample is selected from the group consisting of bone tissue biopsy, bone marrow aspirates, and joint fluids.

55. A method of screening for agents useful for the treatment of bone related disorders, comprising a) contacting agent with a cultured host cell genetically engineered to express PAIGB gene, wherein the PAIGB gene encodes a polypeptide of Claim 8 and b) detecting a change in the expression of PAIGB gene, PAIGB mRNA or PAIGB polypeptide levels.

56. The method of Claim 55, wherein, the agent induces the functional activity of the bone cell.

57. The method of Claim 56 wherein, the functional activity of the bone is induced by inducing the expression of bone specific cells.

58. The method of Claim 55 wherein, the agent is bone anabolic agent.

59. A method for evaluating the efficacy of a treatment of a bone related disorder, in a subject, comprising: for a subject treated with a given protocol; assessing the expression level of a PAIGB nucleic acid molecule defined in Claim 1 or PAIGB polypeptide of Claim 8 wherein a change in the expression level of PAIGB nucleic acid or PAIGB polypeptide after the treatment, relative to the level before the treatment, is indicative of the efficacy of the treatment of a bone disorder.

60. A method for identifying polypeptides, capable of binding to PAIGB, comprising applying a mammalian two-hybrid procedure in which a sequence encoding said PAIGB is carried by one hybrid vector and sequence from a cDNA or genomic DNA library is carried by the second hybrid vector, the vectors then being used to transform the host cell and the positive transformed cells being isolated, followed by extraction of the said second hybrid vector to obtain a sequence encoding a polypeptide which binds to said PAIGB.

61. A method for monitoring the effectiveness of treatment of a subject with a bone related agent comprising the steps of (a) obtaining a pre-administration sample from a subject prior to administration of the agent; (b) detecting the level of expression of a PAIGB protein, mRNA, or genomic DNA in the pre-administration sample; (c) obtaining one or more post-administration samples from the subject; (d) detecting the level of expression or activity of the PAIGB protein, mRNA, or genomic DNA in the post-administration samples; (e) comparing the level of expression or activity of the PAIGB protein, mRNA, or genomic DNA in the pre-administration sample with the PAIGB protein, mRNA, or genomic DNA in the post administration

sample or samples; and (f) altering the administration of the agent to the subject accordingly.

62. A transgenic animal comprising the DNA of Claim 1.

63. The transgenic animal of Claim 62, wherein the animal is a rodent.

64. The transgenic animal of Claim 62, wherein the animal is a mouse.

65. The transgenic animal of Claim 62, wherein the animal is a rat.

66. A transgenic animal of Claim 62 having somatic and/or germ cells comprising a nucleic acid which comprises a promoter region capable of directing protein expression in animal and/or human cells that is operatively linked to a sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 1, 3, 5, 7, or 9 or fragments thereof.

67. A transgenic animal of Claim 62 having somatic and/or germ cells and comprising a nucleic acid which comprises a sequence which encodes polypeptide of Claim 6 and wherein the nucleic acid further comprises an operatively linked promoter region capable of directing protein expression in animal and/or human cells.

68. A transgenic animal of Claim 62 having somatic and/or germ cells comprising a nucleic acid which comprises a promoter region that directs protein expression in animal and/or human cells operatively linked to a sequence comprising at least 15 contiguous nucleotides of SEQ ID NO: 1, 3, 5, 7, or 9, wherein bone mass is modulated relative to non-transgenic animals of the same species in more than one bone parameter.

69. The transgenic animal of Claim 62, wherein the transgenic animal expresses a human PAIGB polypepetide.

70. The transgenic animal of Claim 69, wherein the human PAIGB polypeptide is expressed highest in bone tissue.

71. The transgenic animal of Claim 62, which exhibits a bone phenotype.

72. The transgenic animal of Claim 62, wherein bone mass is modulated relative to a non-transgenic animal of the same species in more than one parameter selected from among bone density, bone strength, trabecular number, bone size, and bone tissue connectivity.

73. An animal model for the study of bone density modulation comprising a first group of animals composed of the transgenic animal of Claim 62 and a second group of control animals.

74. A transgenic mouse having a genome comprising an alteration of the gene encoding PAIGB wherein the alteration is caused by the introduction of a nucleic acid for gene targeting by homologous recombination into embryonic stem cells or pluripotent cells comprising a first section homologous to mouse PAIGB gene and a second section homologous to another section of mouse PAIGB gene, and between the first and the second section a middle section comprising an engineered deletion of a portion of the PAIGB gene, a nucleic acid sequence change, or a nucleic acid insertion, and wherein the nucleic acid is capable of homologous recombination with the endogenous gene.

75. The transgenic mouse of Claim 74, wherein the middle section of the nucleic acid for gene targeting comprises an engineered deletion of the ATG start codon, an engineered frame-shift mutation, an engineered stop codon, a neomycin resistance sequence, a loop recombination site, or a synthetic transcriptional pause sequence.

76. The transgenic mouse of Claim 74, wherein the nucleic acid for gene targeting further comprises both intron and exon sequences of the mouse PAIGB gene.

77. A transgenic animal wherein the expression of endogenous PAIGB is modulated by an altered gene control sequence introduced by homologous or non homologous recombination.

78. The transgenic animal of Claim 62 wherein the PAIGB gene is inducible.

79. A transgenic animal according to Claim 62 wherein said animal is a "Knock-out" animal in which one or both copies of one of the animal's PAIGB genes have been partially or completely deleted by homologous recombination or gene targeting, or have been inactivated by the insertion or substitution by homologous recombination or gene targeting of exogenous sequences.

80. A method for studying bone mass determinants comprising the steps of: (a) providing a first group of transgenic animals according to Claim 1; and (b) measuring at least one parameter of bone development in the transgenic animals.

81. A method for studying the modulation of bone mass comprising the steps of: (a) providing a first group of transgenic animals according to Claim 1; (b) administering a test compound or an experimental procedure; and (c) measuring at least one parameter of bone development in the transgenic animals administered a test compound.

82. A method for studying an effect of PAIGB on bone disorders comprising the steps of: (a) providing embryos of animals with a bone related disorder phenotype; (b) introducing the nucleic acid any one of Claim 1 into a first group of the embryos; (c) transferring the embryos to pseudopregnant mice; and (d) measuring at least one parameter of development in the resultant mice.

83. A method for identifying an agent effective for the treatment of bone related disorders comprising administering said agent to a transgenic animal

according to Claim 62, measuring PAIGB expression in cells of said animal, and comparing PAIGB expression to that in untreated control animals.

84. The method of Claim 83, wherein said agent is administered in combination with other bone related agents.

85. A method for identifying whether an agent, which has bone-forming activity comprising steps of: a) administering the agent to the transgenic animal of Claim 61; and b) examining the transgenic animal after the administration of the agent to determine whether BMD of the animal has been changed.

86. The method of Claim 85, wherein said agent is administered in combination with other bone related agents.

87. A method of Claim 86 wherein the combined administration results in increased bone mineral density.

88. A stably transfected cell line comprising two constructs, the first construct comprising a ligand binding domain linked to a DNA binding domain which is linked to an activation domain all of which expression Is driven by a constitutive promoter, the second construct comprising multiple copies of DNA binding elements linked to a minimal promoter which is linked to PAIGB cDNA, wherein upon the addition of chemical inducer, transcription of PAIGB gene is induced.